
Genome-wide analysis of translation reveals a critical role for deleted in azoospermia-like (Dazl) at the oocyte-to-zygote transition.

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Public Summary:

Oocytes represent the start material for all mammalian development. With the introduction of DNA from the sperm, the oocyte is transformed into a totipotent cell that gives rise to all tissues of the body and the placenta. Therefore, understanding how the oocyte works will give great insight what is required to realize the full developmental potential of any cell. Here, we begin to dissect mechanisms that make the oocyte so unique. We find a protein that had previously been implicated in male infertility is also required for the late female germ cell, the oocyte. In its absence, the oocyte cannot mature. Furthermore, we show that this protein regulates hundreds of genes by inducing their encoded RNAs to produce protein. This fundamental mechanism is likely to be used over and over again in human development. Therefore, these experiments provide a start point for tackling similar questions in stem cells in general.

Scientific Abstract:

Oocyte maturation, fertilization, and early embryonic development occur in the absence of gene transcription. Therefore, it is critical to understand at a global level the post-transcriptional events that are driving these transitions. Here we used a systems approach by combining polysome mRNA profiling and bioinformatics to identify RNA-binding motifs in mRNAs that either enter or exit the polysome pool during mouse oocyte maturation. Association of mRNA with the polysomes correlates with active translation. Using this strategy, we identified highly specific patterns of mRNA recruitment to the polysomes that are synchronized with the cell cycle. A large number of the mRNAs recovered with translating ribosomes contain motifs for the RNA-binding proteins DAZL (deleted in azoospermia-like) and CPEB (cytoplasmic polyadenylation element-binding protein). Although a Dazl role in early germ cell development is well established, no function has been described during oocyte-to-embryo transition. We demonstrate that CPEB1 regulates Dazl post-transcriptionally, and that DAZL is essential for meiotic maturation and embryonic cleavage. In the absence of DAZL synthesis, the meiotic spindle fails to form due to disorganization of meiotic microtubules. Therefore, Cpeb1 and Dazl function in a progressive, self-reinforcing pathway to promote oocyte maturation and early embryonic development.

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